**Title: Changes to An Approved Protocol**
**Standard Operating Procedure # 12**
**Department: Human Research Protection Program/Institutional Review Board**
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**Revision Date:**

**Subject:** Changes To An Approved Study (Modifications/Amendments)

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**Policy:**
All changes to previously approved research, during the period of one year or less for which approval is authorized, require IRB review and approval prior to initiation of the change.

**Procedures:**
Investigators are required to submit to the IRB, for review and approval, any proposed changes to IRB-approved research prior to initiation of the changes. This requirement is stated in the IRB approval letter issued for all new and continuing approved studies. The only exception to this requirement is when a change is necessary to eliminate apparent immediate hazards to the subject. In such a case, the IRB should be promptly informed of the change following its implementation and should review the change to determine that it is consistent with ensuring the subjects' continued welfare.

The IRB Chair and/or the Administrator is/are responsible for reviewing and determining whether the proposed change is minor or substantive in nature. This determination will dictate the level of review required, whether full committee or expedited review.

**Minor Changes:**
Minor changes involve procedures that are no more than minimal risks, or risks to subjects are not increased, and/or the change is not a significant alteration of the study design. Minimal risk means that the probability and magnitude of harm or discomfort anticipated in the research are not greater than those ordinarily encountered in daily life or during the performance of routine physical or psychological examinations or tests. The IRB Chair/Administrator may request additional information from the PI to make this determination. The IRB can use the "expedited" review procedure (review conducted by the IRB Chair or IRB Administrator) to review and approve minor changes. Minor changes include but are not limited to:

1. The addition of research activities that would be considered exempt or expedited if considered independent from the main research protocol;

2. Changes in Principal Investigator or other research personnel;

3. A minor increase or decrease in the number of participants;

4. Narrowing the inclusion criteria;

5. Broadening the exclusion criteria;

6. Changes to the dosage form (e.g., tablet to capsule or oral liquid) of an administered drug when the dose and route of administration remain constant;

7. Decreasing the number of biological sample collections, provided that such a change does not affect the collection of information related to safety evaluations;

8. An increase in the number of study visits for the purpose of increased safety monitoring;

9. A decrease in the number of study visits, provided the decrease does not affect the collection of information related to safety evaluations;

10. Changes in remuneration;

11. Changes to improve the clarity of statements or to correct typographical errors, provided that such a change does not alter the content or intent of the statement;

12. The addition or deletion of qualified investigators;

13. The addition or deletion of study sites.

**Substantive Changes:**
Any change to a study that involves increased risk to subjects or significantly affects the nature of the study must be reviewed by the full IRB Committee. Examples may include changes to the recruitment plan, adding or revising eligibility criteria, adding a research site, or changing the consent form to include a newly identified side effect or adverse event related to the study drug. Changes that are not minor are scheduled for review by the full IRB Committee at a convened meeting.

**Submission of Proposed Changes to the IRB**:
Proposed changes to a study are submitted to the IRB using the Modification/Amendment Form provided by the IRB administration. The form must include a description of and justification for the proposed change(s) and information about any change in the level of risk to the study participants. The form also includes a series of questions to assist in making the determination whether the proposed change is minor or substantive.

**Review Procedures:**
Expedited Review and Approval—The IRB Chair/IRB Administrator reviews the Modification/ Amendment Form. The researcher should address on the form the reason for the change and how it will change the study. When the change has been approved, the approval will be documented on the Modification/Amendment Form and will be sent to the researcher. A copy will be placed in the official IRB record of the study. Researchers must ensure that a copy of the complete documentation and IRB approval be placed in the research record and be available for inspection.

Under expedited review, a change cannot be disapproved; however, the IRB Chair/IRB Administrator can recommend that the change be reviewed by the full IRB Committee. The IRB Chair/IRB Administrator will review the materials to determine the level of review required.

Federal regulations require that all IRB members be informed of all changes to ongoing research approved through the expedited review procedure. The IRB administration satisfies this requirement by inclusion of this information on all IRB Committee agendas and include it as a discussion item at the convened meeting of the Board.

Full Board Review and Approval—When the change is substantive, that is, it increases risks to participants beyond minimal risk, or is a significant change in the study design, the change must be reviewed by the full IRB. The review will follow the IRB's procedure for full-board review and will appear on the agenda of the IRB Committee Meeting. The researcher should address on the Modification/Amendment Form the reason for the change, how it will change the study, how it will affect the risks to the study participants, and what safeguards will be implemented to protect the study participants from the additional risks. It should include information about how the change will affect currently enrolled study participants. If appropriate, the researcher should provide references to support the change. If the change involves a revision to the Consent Form, a revised Consent Form must be submitted to the full IRB. The IRB should determine whether the change affects previously enrolled study participants and whether it might affect their willingness to continue in the study. If so, study participants should be contacted and presented with a revised Consent Form.

After IRB review, the Committee will vote on the proposed change(s). When the change has been approved by the full IRB, the approval will be documented on the Modification/ Amendment Form and will be sent to the researcher. A copy will be placed in the official IRB record of the study. Researchers must ensure that a copy of the complete documentation and IRB approval be placed in the research record and be available for inspection.

**References:**

*45 CFR 46.110(b)(2)(c)*
*Institutional Review Board Management and Function, Elizabeth A. Bankert and Robert J. Amdur, Chapter 7, Revisions to An Approved Study*